# Ethylene Glycol Monoethyl Ether (2-Ethoxyethanol)

CAS #110-80-5
Swiss CD-1 mice, at 0.0, 0.5, 1.0, 2.0%, drinking water
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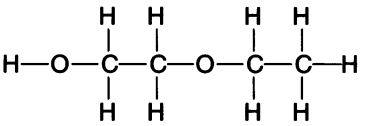

Ethylene glycol monoethyl ether (EGEE), a common chemical and solvent used in industry and in consumer goods, was tested for reproductive toxicity in Swiss CD-1 mice using the RACB protocol (Lamb et al., Environ Health Perspect 57:85–90 [1984]). It was part of a series of glycol ethers and congeners evaluated for structure–activity correlations using this design. Data collected on body weights, clinical signs, and food and water consumption during the dose-range-finding segment (Task 1) were used to set concentrations for the main study (Task 2) at 0.5, 1.0, and 2.0% weight per volume EGEE in drinking water. These concentrations produced calculated consumption estimates of approximately 0.76, 1.50, and 2.6 g/kg/day.

There were no effects on body weights during the continuous cohabitation portion of the study. Two females died in both the control and high dose groups. Water consumption was unchanged by the addition of EGEE.

No pairs in the 2% EGEE group had any litters of pups, live or dead. In the middle dose group (1% EGEE), the number of litters per fertile pair was reduced by 35%, there were approximately 2.6 live pups per litter versus a control mean of 9.8, the proportion of pups born alive was reduced by 50%, and the weight of the live pups, adjusted for litter size, was reduced by 12%. The fertility indices in the low dose (0.5% EGEE) were not affected.

Task 3 crossover mating trials were conducted with the controls and both the 2% EGEE and 1% EGEE groups. With the 2% EGEE mice, no litters were delivered of treated females mated with control males, while 5 of 18 control females delivered a litter after mating with a treated male (significantly less than the 17 of 20 control × control matings). The proportion born alive, the sex ratio, and the adjusted live pup weight were not affected when one parent had been exposed to 2% EGEE.

For the 1% EGEE mice, 78% of control pairs were fertile (bore any young), while only 44% of matings were fertile if the male had consumed 1% EGEE. The fertility of treated females × control male matings was not different from that of controls. Litters from control dams mated with treated males were not different from controls, while litters from treated females × control males had pups that were 12% lighter than controls, when adjusted for litter size.

After the last Task 3 mating, and 7 days of lavage for vaginal cytology, the $F_0$ mice from the control, 1 and 2% EGEE groups were killed and necropsied. The 15% reduction in female body weight at 2% EGEE may be related to the fact that these animals never were pregnant. Adjusted liver weight was increased in the 1% EGEE-treated females females, while adjusted brain weight was decreased in 2% EGEE-treated females by 10%. In males, liver weight was unchanged, while adjusted brain weight was decreased by 5 and 8% in the 1% EGEE and 2% EGEE groups, respectively. Absolute testis weights in the middle and high dose groups were reduced by 11 and 35%, respectively. Relative epididymis and seminal vesicle weights were reduced in the 2% EGEE group by 18 and 12%, respectively. Abnormal sperm forms were increased by approximately 2.5-fold at 1% EGEE, and by approximately 13-fold at 2% EGEE from a control value of 3.3%. Also at 2% EGEE, sperm motility was reduced by 40% and epididymal sperm density was down by 19%. In the 2% EGEE group, vaginal cycle length was increased to 5.5 days, from a control value of 4.6 days.

An analysis of the second generation was not conducted in this study.

In conclusion, ethylene glycol monoethyl ether was clearly toxic to reproduction in both $F_0$ male and female mice at 1 and 2% in drinking water, based on reduced pup numbers and weight in Task 2, fertility and pup weight effects in Task 3, and alterations in estrous cyclicity and epididymal sperm parameters at necropsy.

**Summary:** NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: **PB85118651**
Chemical: **Ethylene Glycol Monoethyl Ether (2-Ethoxyethanol)**
CAS#: **110-80-5**
Mode of exposure: **Drinking water**
Species/strain: **Swiss CD-1 mice**

| $F_0$ generation — Dose concentration → | 0.5% | 1.0% | 2.0% |
|---|---|---|---|
| General toxicity | Male, female | Male, female | Male, female |
| Body weight | —, — | —, — | ↓, — |
| Kidney weight[a] | •, • | •, • | •, • |
| Liver weight[a] | •, • | —, ↑ | —, — |
| Mortality | —, — | —, — | —, — |
| Feed consumption | •, • | •, • | •, • |
| Water consumption | —, — | —, — | —, — |
| Clinical signs | —, — | —, — | —, — |
| **Reproductive toxicity** | | | |
| x̄ litters/pair | — | ↓ | ↓ |
| # live pups/litter; pup wt./litter | —, — | ↓, ↓ | +, + |
| Cumulative days to litter | — | ↑ | + |
| Absolute testis, epididymis weight[a] | •, • | ↓, ↓ | ↓, ↓ |
| Sex accessory gland weight[a] (prostate, seminal vesicle) | • | —, — | —, ↓ |
| Epidid. sperm parameters (#, motility, morphology) | • | —, —, ↑ | ↓, ↓, ↑ |
| Estrous cycle length | • | — | ↑ |

| Determination of affected sex (crossover) | Male | Female | Both |
|---|---|---|---|
| Dose level | — | — | 1.0 and 2.0% |

| $F_1$ generation — Dose concentration → | 0.5% | 1.0% | 2.0% |
|---|---|---|---|
| General toxicity | Male, female | Male, female | Male, female |
| Pup growth to weaning | • | • | • |
| Mortality | • | • | • |
| Adult body weight | • | • | • |
| Kidney weight[a] | • | • | • |
| Liver weight[a] | • | • | • |
| Feed consumption | • | • | • |
| Water consumption | • | • | • |
| Clinical signs | • | • | • |
| **Reproductive toxicity** | | | |
| Fertility index | • | • | • |
| # live pups/litter; pup wt./litter | •, • | •, • | •, • |
| Absolute testis, epididymis weight[a] | •, • | •, • | •, • |
| Sex accessory gland weight[a] (prostate, seminal vesicle) | •, • | •, • | •, • |
| Epidid. sperm parameters (#, motility, morphology) | •, •, • | •, •, • | •, •, • |
| Estrous cycle length | • | • | • |

| Summary information | |
|---|---|
| Affected sex? | Both |
| Study confounders: | None |
| NOAEL reproductive toxicity: | 0.5% |
| NOAEL general toxicity: | 0.5% |
| $F_1$ more sensitive than $F_0$? | Unclear |
| Postnatal toxicity: | Unclear |

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change ($p<0.05$); — , —, no change in males or females; +, no litters of live pups to evaluate.
[a]Adjusted for body weight.